Supplementary Online Content

Muntner P, Colantonio LD, Cushman M, et al. Validation of the atherosclerotic cardiovascular disease pooled cohort risk equations. *JAMA*. doi:10.1001/jama.2014.2630

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eFigure. Inclusion criteria applied to the REasons for Geographic and Racial Differences in Stroke (REGARDS) study for the validation of the Pooled Cohort risk equations

References

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Estimation of race- and gender-specific ASCVD risk using the ASCVD Pooled Cohort risk equations[1]

	$S_0(t)$ at 5 years†	$S_0(t)$ at 10 years	Mean score	Equations parameters*
				Individual score
Participants not taking antihypertensive medications				
Black women	0.98194	0.9533	86.61	= 17.114 × ln(age) + 0.94 × ln(TC) - 18.92 × ln(HDL-C) + 4.475 × ln(age) × ln(HDL-C) + 27.82 × ln(SBP) - 6.087 × ln(age) × ln(SBP) (+ 0.691 if current smoker) (+ 0.874 if diabetes)
White women	0.98898	0.9665	-29.18	= - 29.799 × ln(age) + 4.884 × ln(age)^2 + 13.54 × ln(TC) - 3.114 × ln(age) × ln(TC) -13.578 × ln(HDL-C) + 3.149 × ln(age) × ln(HDL-C) + 1.957 × ln(SBP) (+ 7.574 - 1.665 × ln(age) if current smoker) (+ 0.661 if diabetes)
Black men	0.95726	0.8954	19.54	= 2.469 × ln(age) + 0.302 × ln(TC) - 0.307 × ln(HDL-C) + 1.809 × ln(SBP) (+ 0.549 if current smoker) (+ 0.645 if diabetes)
White men	0.96254	0.9144	61.18	= 12.344 × ln(age) + 11.853 × ln(TC) - 2.664 × ln(age) × ln(TC) - 7.99 × ln(HDL-C) + 1.769 × ln(age) × ln(HDL-C) + 1.764 × ln(SBP) (+ 7.837 - 1.795 × ln(age) if current smoker) (+ 0.658 if diabetes)
Participants taking antihypertensive medications				
Black women	0.98194	0.9533	86.61	= 17.114 × ln(age) + 0.94 × ln(TC) - 18.92 × ln(HDL-C) + 4.475 × ln(age) × ln(HDL-C) + 29.291 × ln(SBP) - 6.432 × ln(age) × ln(SBP) (+ 0.691 if current smoker) (+ 0.874 if diabetes)
White women	0.98898	0.9665	-29.18	= - 29.799 × ln(age) + 4.884 × ln(age)^2 + 13.54 × ln(TC) - 3.114 × ln(age) × ln(TC) -13.578 × ln(HDL-C) + 3.149 × ln(age) × ln(HDL-C) + 2.019 × ln(SBP) (+ 7.574 - 1.665 × ln(age) if current smoker) (+ 0.661 if diabetes)
Black men	0.95726	0.8954	19.54	= 2.469 × ln(age) + 0.302 × ln(TC) - 0.307 × ln(HDL-C) + 1.916 × ln(SBP) (+ 0.549 if current smoker) (+ 0.645 if diabetes)
White men	0.96254	0.9144	61.18	= 12.344 × ln(age) + 11.853 × ln(TC) - 2.664 × ln(age) × ln(TC) - 7.99 × ln(HDL-C) + 1.769 × ln(age) × ln(HDL-C) + 1.797 × ln(SBP) (+ 7.837 - 1.795 × ln(age) if current smoker) (+ 0.658 if diabetes)

ASCVD: atherosclerotic cardiovascular disease; HDL-C: high-density lipoprotein cholesterol; REGARDS: REasons for Geographic And Racial Differences in Stroke; SBP: systolic blood pressure; TC: total cholesterol.

* Final risk estimation is calculated as:

$$Predicted\ ASCVD\ risk = 1 - S_0(t)^{e^{(Individual\ score - Mean\ score)}}$$

† Obtained from the ACC/AHA Guideline on the Assessment of Cardiovascular Risk working group (S. Coady, Personal Communication).

eTable 2. Baseline characteristics of the REGARDS population included in the study

	REGARDS data only		REGARDS-Medicare linked data	
	Overall population	Participants without diabetes, LDL-C 70 to 189 mg/dL,* not taking statins	Overall population	Participants without diabetes, LDL-C 70 to 189 mg/dL,* not taking statins
Participants, *n*	*18,498*	*10,997*	*6,121*	*3,333*
Age (years), mean (SD)	62.6 (8.1)	61.9 (8.3)	70.6 (4.1)	70.7 (4.1)
Blacks, n (%)	7,705 (41.7)	4,132 (37.6)	2,298 (37.5)	1,095 (32.9)
Men, n (%)	7,724 (41.8)	4,480 (40.7)	2,729 (44.6)	1,476 (44.3)
Region of residence,[†] %				
Stroke buckle	3,909 (21.1)	2,255 (20.5)	1,175 (19.2)	584 (17.5)
Stroke belt	6,475 (35.0)	3,870 (35.2)	2,123 (34.7)	1,189 (35.7)
Other contiguous US states	8,114 (43.9)	4,872 (44.4)	2,823 (46.1)	1,560 (46.8)
Less than high school, %	1,871 (10.1)	898 (8.2)	813 (13.3)	349 (10.5)
No physical activity, %	5,709 (31.3)	3,213 (29.6)	1,950 (32.4)	1,004 (30.6)
Current smoking, n (%)	2,670 (14.4)	1,626 (14.8)	621 (10.2)	348 (10.4)
Diabetes, n (%)	3,296 (17.8)	-	1,170 (19.1)	-
BMI, median (25th-75th percentile)	28.4 (25.1-32.6)	27.6 (24.5-31.5)	27.9 (24.7-31.6)	27.1 (24.1-30.6)
SBP (mmHg), mean (SD)	126.2 (16.4)	124.8 (15.9)	129.1 (16.2)	128.3 (16.2)
Taking antihypertensive medication, n (%)	8,760 (47.4)	4,134 (37.6)	3,297 (53.9)	1,491 (44.7)
3 or more antihypertensive medication classes, n (%)	1,948 (10.5)	682 (6.2)	830 (13.6)	283 (8.5)
TC (mg/dL), mean (SD)	195.8 (38.8)	202.6 (31.0)	192.9 (38.2)	202.4 (30.8)
HDL-C (mg/dL), mean (SD)	52.9 (16.2)	54.1 (16.5)	53.3 (16.4)	54.7 (16.9)
LDL-C (mg/dL),[‡] mean (SD)	118.0 (34.0)	124.5 (26.9)	115.0 (33.5)	123.5 (26.4)
Statin use, n (%)	4,627 (25.0)	-	1,860 (30.4)	-
CRP, median (25th-75th percentile)	2.2 (0.9-4.9)	2.1 (0.9-4.7)	2.1 (1.0-4.6)	2.1 (1.0-4.6)
eGFR < 60 ml/min/$1.73m^2$, n (%)	1,362 (7.4)	576 (5.2)	782 (12.8)	333 (10.0)
ACR ≥ 30 mg/g, n (%)	2,092 (11.7)	906 (8.5)	808 (13.7)	340 (10.6)

ACR: albumin-to-creatinine ratio; BMI: body mass index; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; REGARDS: REasons for Geographic And Racial Differences in Stroke; SBP: systolic blood pressure; SD: standard deviation; TC: total cholesterol.

* Non-HDL cholesterol between 100 and 219 for the 1,255 who had not fasted prior to their REGARDS study visit.
[†] Stroke buckle includes coastal North Carolina, South Carolina and Georgia. Stroke belt includes the remaining parts of North Carolina,

South Carolina and Georgia and Tennessee, Mississippi, Alabama, Louisiana and Arkansas.
‡ LDL-C values were available for participants who fasted prior to their REGARDS study visit.

eTable 3. Observed and predicted atherosclerotic cardiovascular disease events in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study by decile of risk, overall (n=18,498, top panel), and among participants without diabetes, with LDL-C 70-189 mg/dL and not taking statins (n=10,997, bottom panel)

Decile of Predicted risk	Events / participants	Events in 5-years Observed KM-adjusted	Predicted	5-years incidence rate* Observed KM-adjusted	Predicted	Calibration Chi-squared (p-value)	Discrimination C-index (95% CI)
All participants						84.2 (<0.001)	0.71 (0.69-0.72)
<2.3%	4 / 1,849	4.5	8.7	0.5 (0.2-1.3)	0.9		
2.3% to <4.1%	23 / 1,850	26.6	21.3	2.9 (1.9-4.3)	2.3		
4.1% to <6.1%	27 / 1,850	31.1	35.0	3.4 (2.3-4.9)	3.8		
6.1% to <8.0%	40 / 1,850	46.7	50.2	5.0 (3.7-6.9)	5.4		
8.0% to <10.3%	42 / 1,850	50.7	66.4	5.5 (4.0-7.4)	7.2		
10.3% to <12.9%	68 / 1,850	76.1	85.8	8.2 (6.5-10.4)	9.3		
12.9% to <16.2%	78 / 1,850	89.9	109.1	9.7 (7.8-12.1)	11.8		
16.2% to <20.5%	104 / 1,850	118.5	139.2	12.8 (10.6-15.5)	15.0		
20.5% to <27.5%	110 / 1,850	129.4	184.8	14.0 (11.7-16.8)	20.0		
≥27.5%	178 / 1,849	199.6	313.1	21.7 (18.8-25.0)	33.9		
Participants without diabetes, LDL-C 70 to 189 mg/dL,†, not taking statins						19.9 (0.01)	0.72 (0.70-0.75)
<1.8%	4 / 1,099	4.5	4.1	0.8 (0.3-2.2)	0.8		
1.8% to <3.2%	6 / 1,100	6.1	9.8	1.1 (0.5-2.5)	1.8		
3.2% to <4.8%	16 / 1,100	18.5	16.0	3.4 (2.1-5.5)	2.9		
4.8% to <6.5%	18 / 1,100	21.8	23.6	4.0 (2.5-6.3)	4.3		
6.5% to <8.3%	25 / 1,099	29.0	31.5	5.3 (3.6-7.8)	5.7		
8.3% to <10.5%	28 / 1,100	33.6	40.8	6.1 (4.2-8.8)	7.4		
10.5% to <13.1%	36 / 1,100	40.3	52.2	7.3 (5.3-10.1)	9.5		
13.1% to <16.4%	38 / 1,100	43.6	66.1	7.9 (5.8-10.8)	12.0		
16.4% to <21.7%	60 / 1,100	68.2	86.2	12.4 (9.7-15.9)	15.7		
≥21.7%	107 / 1,099	123.3	136.2	22.5 (18.7-26.9)	24.8		

95% CI: 95% confidence interval. HDL: high density lipoprotein; KM: Kaplan-Meier; LDL-C: low density lipoprotein cholesterol.

* Per 1,000 person-years.

† Non-HDL cholesterol between 100 and 219 for the 1,255 who had not fasted prior to their REGARDS study visit.

eTable 4. Observed and predicted incidence rates of atherosclerotic cardiovascular disease in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study by 10-year predicted risk, overall population (top panel), and among participants without diabetes, with LDL-C 70-189 mg/dL and not taking statins (bottom panel)

	Events / participants	Events in 5-years		5-year incidence rate*		Calibration	Discrimination
		Observed KM-adjusted	Predicted	Observed KM-adjusted (95% CI)	Predicted	Chi-squared (p-value)	C-index (95% CI)
Overall population							
10-year predicted risk		**Belt region (n=10,384)**				39.2 (<0.001)	0.73 (0.70-0.75)
<5%	20 / 2,711	23.7	26.3	1.8 (1.1-2.8)	1.9		
5% to <7.5%	27 / 1,363	31.1	32.4	4.6 (3.1-6.6)	4.8		
7.5% to <10%	23 / 1,140	28.3	38.7	5.0 (3.3-7.5)	6.8		
≥10%	300 / 5,170	341.7	457.8	13.3 (11.9-14.8)	17.7		
10-year predicted risk		**Non-belt region (n=8,114)**				61.2 (<0.001)	0.68 (0.65-0.71)
<5%	24 / 1,868	27.7	18.4	3.0 (2.0-4.4)	2.0		
≥5% to <7.5%	15 / 980	17.9	23.6	3.7 (2.2-6.1)	4.8		
≥7.5% to <10%	25 / 972	28.9	33.5	5.9 (4.0-8.8)	6.9		
≥10%	240 4,294	272.3	382.8	12.7 (11.2-14.4)	17.8		
Participants without diabetes, with LDL-C 70 to 189 mg/dL[†] who were not taking statins							
10-year predicted risk		**Belt region (n=6,125)**				14.9 (0.06)	0.73 (0.70-0.76)
<5%	11 / 2,027	12.8	19.1	1.3 (0.7-2.3)	1.9		
5% to <7.5%	21 / 897	24.4	21.4	5.4 (3.5-8.3)	4.8		
7.5% to <10%	18 / 703	22.1	24.1	6.3 (3.9-10.0)	6.8		
≥10%	133 / 2,498	153.6	186.7	12.3 (10.4-14.5)	14.9		
10-year predicted risk		**Non-belt region (n=4,872)**				24.1 (0.002)	0.71 (0.67-0.75)
<5%	17 / 1,426	19.4	13.6	2.7 (1.7-4.4)	1.9		
≥5% to <7.5%	11 / 681	13.3	16.4	3.9 (2.1-7.0)	4.8		
≥7.5% to <10%	16 / 629	18.7	21.6	5.9 (3.6-9.7)	6.9		
≥10%	111 / 2,136	124.9	163.6	11.7 (9.7-14.0)	15.3		

Predicted risk determined using the Pooled Cohort risk equations. 95% CI: 95% confidence interval. KM: Kaplan-Meier.
* Per 1,000 person-years.

† Non-HDL cholesterol between 100 and 219 for the 1,255 who had not fasted prior to their REGARDS study visit.

eTable 5. Baseline characteristics of REGARDS participants linked to Medicare claims according to 10-year predicted atherosclerotic cardiovascular disease risk, overall (n=6,121, top panel), and among participants without diabetes, with LDL-C 70 to 189 mg/dL and who were not taking statins (n=3,333, bottom panel)

	10-year predicted ASCVD risk – Medicare linked participants			p-trend
	<7.5%	7.5% to <10%	≥10%	
Participants, n (%)	556 (9.1)	558 (9.1)	5,007 (81.8)	-
Age (years), mean (SD)	66.8 (1.7)	68.1 (2.6)	71.3 (4.1)	<0.001
Blacks, n (%)	106 (19.1)	219 (39.3)	1,973 (39.4)	<0.001
Men, n (%)	13 (2.3)	87 (15.6)	2,629 (52.5)	<0.001
Current smoking, n (%)	13 (2.3)	27 (4.8)	581 (11.6)	<0.001
Diabetes, n (%)	N<11 (suppressed)	(suppressed)	1,154 (23.1)	<0.001
SBP (mmHg), mean (SD)	114.7 (11.8)	120.7 (11.2)	131.7 (15.9)	<0.001
Antihypertensive medication, n (%)	133 (23.9)	234 (41.9)	2,930 (58.5)	<0.001
TC (mg/dL), mean (SD)	193.5 (35.6)	193.1 (34.6)	192.8 (38.8)	0.69
HDL-C (mg/dL), mean (SD)	63.0 (17.0)	57.2 (15.8)	51.8 (16.0)	<0.001
LDL-C (mg/dL), mean (SD)	108.5 (30.6)	113.1 (30.4)	116.0 (34.1)	<0.001
Statin use, n (%)	165 (29.7)	156 (28.0)	1,539 (30.7)	0.24
Participants without diabetes, LDL-C 70 to 189 mg/dL,[†] not taking statins				
10-year predicted ASCVD risk – Medicare linked participants				
	<7.5%	7.5% to <10%	≥10%	
Participants, n (%)	352 (10.6)	366 (11.0)	2,615 (78.4)	-
Age (years), mean (SD)	66.7 (1.7)	67.9 (2.5)	71.6 (4.1)	<0.001
Blacks, n (%)	56 (15.9)	145 (39.6)	894 (34.2)	<0.001
Men, n (%)	N<11 (suppressed)	(suppressed)	1,408 (53.8)	<0.001
Current smoking, n (%)	N<11 (suppressed)	(suppressed)	321 (12.3)	<0.001
SBP (mmHg), mean (SD)	114.5 (12.1)	120.5 (11.5)	131.2 (15.9)	<0.001
Antihypertensive medication, n (%)	69 (19.6)	133 (36.3)	1,289 (49.3)	<0.001
TC (mg/dL), mean (SD)	204.9 (30.1)	202.6 (29.4)	202.0 (31.0)	0.15
HDL-C (mg/dL), mean (SD)	64.1 (16.4)	57.6 (16.0)	53.0 (16.6)	<0.001
LDL-C (mg/dL), mean (SD)	118.7 (25.6)	121.7 (25.9)	124.4 (26.5)	<0.001

N<11 indicates fewer than 11 participants are used in calculating the statistic. These numbers are suppressed per data use agreement with Centers for Medicaid and Medicare Services. Other cells are not presented to prevent calculating actual number in the suppressed cells.
ASCVD: atherosclerotic cardiovascular disease; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; REGARDS: REasons for Geographic And Racial Differences in Stroke; SBP: systolic blood pressure; SD: standard deviation; TC: total cholesterol.
[†] Non-HDL cholesterol between 100 and 219 for the 1,255 who had not fasted prior to their REGARDS study visit.

eTable 6. Observed and predicted ASCVD events in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study participants linked to Medicare claims by decile of risk, overall (n=6,121, top panel), and among participants without diabetes, with LDL-C 70-189 mg/dL and not taking statins (n=3,333, bottom panel)
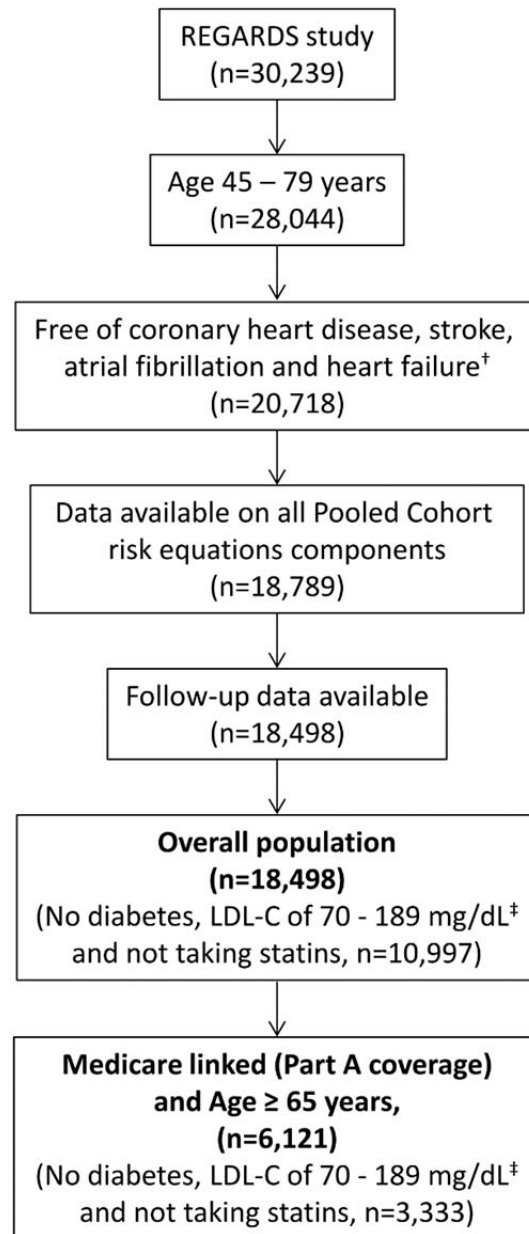
Decile of Predicted risk	Events / participants	Events in 5-years		5-years incidence rate*		Calibration Chi-squared (p-value)	Discrimination C-index (95% CI)
		Observed KM-adjusted	Predicted	Observed KM-adjusted	Predicted		
All participants						11.4 (0.18)	0.65 (0.62-0.67)
<7.8%	17 / 612	17.7	12.9	5.8 (3.6-9.3)	4.2		
7.8% to <10.4%	18 / 612	21.0	20.7	6.8 (4.3-10.8)	6.8		
10.4% to <12.8%	30 / 612	31.3	27.7	10.2 (7.2-14.5)	9.1		
12.8% to <15.0%	33 / 612	35.1	33.7	11.6 (8.3-16.1)	11.0		
15.0% to <17.4%	44 / 612	47.2	40.3	15.4 (11.5-20.4)	13.2		
17.4% to <20.0%	41 / 613	43.8	47.1	14.3 (10.6-19.2)	15.4		
20.0% to <23.2%	52 / 612	56.1	55.2	18.3 (14.1-23.7)	18.0		
23.2% to <27.5%	50 / 612	54.5	65.6	17.8 (13.6-23.2)	21.4		
27.5% to <34.7%	75 / 612	80.6	82.5	26.3 (21.3-32.5)	27.0		
≥34.7%	97 / 612	104.9	127.8	34.2 (28.5-41.0)	41.8		
Participants without diabetes, LDL-C 70 to 189 mg/dL,†, not taking statins						5.4 (0.71)	0.67 (0.64-0.71)
<7.4%	Sup / 333	9.3	6.6	5.6 (2.9-10.6)	3.9		
7.4% to <9.6%	Sup / 333	12.0	10.4	7.2 (4.0-12.9)	6.2		
9.6% to <11.8%	11 / 334	11.9	13.6	7.1 (4.0-12.7)	8.2		
11.8% to <13.7%	13 / 333	13.4	16.7	8.0 (4.7-13.6)	10.0		
13.7% to <15.5%	18 / 333	20.8	19.4	12.4 (7.9-19.4)	11.6		
15.5% to <17.8%	23 / 334	24.3	22.8	14.5 (9.8-21.5)	13.6		
17.8% to <20.1%	24 / 333	25.6	26.0	15.4 (10.4-22.6)	15.6		
20.1% to <23.4%	31 / 334	33.9	30.7	20.3 (14.4-28.3)	18.4		
23.4% to <27.9%	37 / 333	40.3	36.5	24.2 (17.8-32.7)	21.9		
≥27.9%	57 / 333	60.6	51.2	36.3 (28.6-45.8)	30.8		

95% CI: 95% confidence interval. ASCVD: atherosclerotic cardiovascular disease; HDL: high density lipoprotein; KM: Kaplan-Meier; LDL-C: low density lipoprotein cholesterol; Sup: suppressed because cells with n < 11.

* Per 1,000 person-years.

† Non-HDL cholesterol between 100 and 219 for the 1,255 who had not fasted prior to their REGARDS study visit.

eFigure. Inclusion criteria applied to the REasons for Geographic and Racial Differences in Stroke (REGARDS) study for the validation of the Pooled Cohort risk equations


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                    REGARDS study
                     (n=30,239)
                          │
                          ▼
                  Age 45 – 79 years
                     (n=28,044)
                          │
                          ▼
        Free of coronary heart disease, stroke,
         atrial fibrillation and heart failure†
                     (n=20,718)
                          │
                          ▼
        Data available on all Pooled Cohort
           risk equations components
                     (n=18,789)
                          │
                          ▼
              Follow-up data available
                     (n=18,498)
                          │
                          ▼
              Overall population
                 (n=18,498)
      (No diabetes, LDL-C of 70 - 189 mg/dL‡
        and not taking statins, n=10,997)
                          │
                          ▼
         Medicare linked (Part A coverage)
              and Age ≥ 65 years,
                   (n=6,121)
      (No diabetes, LDL-C of 70 - 189 mg/dL‡
        and not taking statins, n=3,333)
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† Heart failure was defined by use of digoxin assessed by pill bottle review during the REGARDS in-home study visit.

‡ Non-HDL cholesterol between 100 and 219 mg/dL was required for the 1,255 participants who did not have a valid LDL-C measurement (i.e., were not fasting prior to their REGARDS study visit or had serum triglycerides > 400 mg/dL).HDL: high density lipoprotein; LDL-C: low density lipoprotein cholesterol.

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